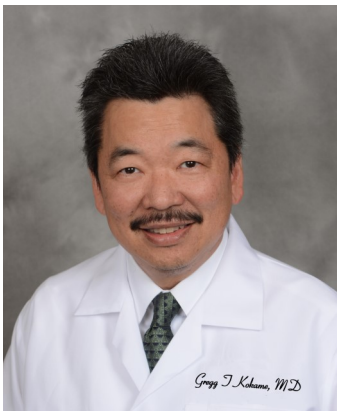
RETINA CONSULTANTS OF HAWAII

Retina Consultants of Hawaii Newsletter VOLUME SIX ISSUE 1—Summer 2017

A Letter from the Medical Director



Mentorship is one of the most important things in all professions, but especially in medicine. The ability to learn from the brightest, most experienced, and creative minds in medicine is one of my most cherished experiences. For me, it was learning from the father of medical retina, J. Donald M. Gass MD. Dr. Gass established medical retina as a field in itself and developed theories of pathogenesis of disease, which continues to resonate today—many years after his passing. His approach to medicine, his incredible enthusiasm for medicine, and his humble personality made him a highly respected figure in retinal diseases—even by other leaders in retina—as well as the ones who were lucky enough to learn from and work with him. The Gass Fellowship Society was established to continue Dr. Gass' work and his approach to medicine. I am honored to continue to help and organize this meeting where the greatest minds in retina come together to discuss challenging cases and continue to better understand the pathophysiology of disease.

Another great mentor is Professor Alan Bird of Moorfields Eye Hospital in London. Moorfields Eye Hospital is one of the most significant eye hospitals in the history of ophthalmology. In 2000, my family and I spent 2 months in London where I had the privilege of doing my sabbatical with Professor Bird. With 20 other fellows from around the world, we learned together from Professor Bird and discussed incredible cases and pathology in retinal diseases.

By having trained with the best minds in the field of retina, the teachings from these incredible mentors stimulated a deep interest in retinal diseases and provided the ability to contribute to our field with world-leading research. In the medical profession there is compassion that we give to our patients, and there is also a compassion that we have for our fellow younger colleagues, who are starting their careers in medicine and in ophthalmology. Because of this, all 3 of our physicians are part of the faculty of the University of Hawaii School of Medicine. We train medical students, transitional interns, and international fellows and provide mentorship to them in their future careers. We thank our patients for their patience as we often do have students with us in our clinics.

To mentor one's colleagues and to help develop the future of ophthalmology for Hawaii is a deeper goal of Retina Consultants of Hawaii, as we believe in the importance of education as one of our core values. Many of our previous students are now practicing ophthalmologists and eye surgeons here in Hawaii, and providing important care to our community. Many of our previous retina fellows are now retinal faculty in the Philippines, Japan, Taiwan, and USA. We also sponsor educational programs in retinal diseases for our community. Next year, we celebrate the 25th anniversary of the educational programs of Retina Consultants of Hawaii. We will not only have well-recognized speakers from around the world, but there will be special presentations from international attendees. The 25th Anniversary Retina Meeting of Retina Consultants of Hawaii will help celebrate our 25th year caring for patients with retinal diseases in Hawaii, as well as highlight our research accomplishments over this quarter of a century. What a fantastic 25 years it has been, but the future for Retina Consultants of Hawaii is even brighter.

Thanks so much again to the doctors and patients of Hawaii for entrusting us with their care.

Best Regards,

Gregg T. Kokame, MD MMM
Medical Director, Hawaii Macula and Retina Institute
Managing Partner, Retina Consultants of Hawaii

HAWAII MACULA AND RETINA INSTITUTE
Revolutionary Research with World-Wide Impact

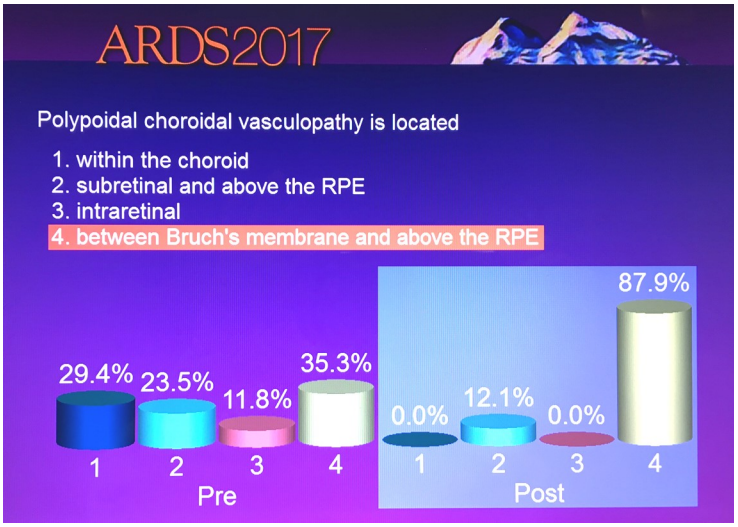
Retina Consultants of Hawaii Research Provides New Insights at Highly Respected Aspen Retina Meeting

Macular degeneration is the leading cause of vision loss in the United States and Europe. Wet macular degeneration leads to leaking and bleeding under the retina, and results in the most frequent cause of severe vision loss. The first two drugs approved by the FDA for treatment of wet macular degeneration underwent their initial pivotal clinical trials at Retina Consultants of Hawaii as the only Hawaii clinical site in the national multi-centered clinical trials, which led to approval by the FDA. These two drugs, Lucentis and Eylea, along with a compounded drug for cancer in the same class named Avastin, now provide the most important means of preventing vision loss and decreasing the leaking and bleeding complications of wet macular degeneration.

However, there is one subtype of subretinal neovascularization or wet macular degeneration that has a higher incidence of resistance to the previously discussed medications. This subtype of polypoidal choroidal vasculopathy (PCV) is more common in Asian populations, so the population of Hawaii provides one of the best regions in the USA to study this disease and its best management. The publications and teachings by Retina Consultants of Hawaii doctors and staff have led to important new information and understanding of PCV. The first step in understanding PCV better is to accurately diagnose this under-recognized disease. The diagnostic studies pioneered here in Hawaii by Retina Consultants of Hawaii have better characterized the findings of PCV with all of the newest diagnostic testing.

Dr. Kokame presenting at 45th Annual Aspen Retinal Detachment Society Meeting on March 27, 2017

At the Aspen Retina Detachment Society meeting in March of 2017, Dr. Gregg Kokame was invited to teach the audience of prominent retinal specialists, many of whom are leaders and chairman of ophthalmology departments in the US, about the newest diagnostic tests for PCV, as well as the most recently released treatment trials specific to PCV. Our OCT studies recently published in the Transactions of the American Ophthalmological Society have localized PCV to the region between Bruch's membrane and the retinal pigment epithelium (RPE). Audience testing initially showed that only 35% of attendees knew this, but after the lecture almost 90% understood this important teaching. This information is important to guide and understand diagnostic testing, such as optical coherence tomography (OCT), en face OCT, OCT angiography, and indocyanine green angiography.



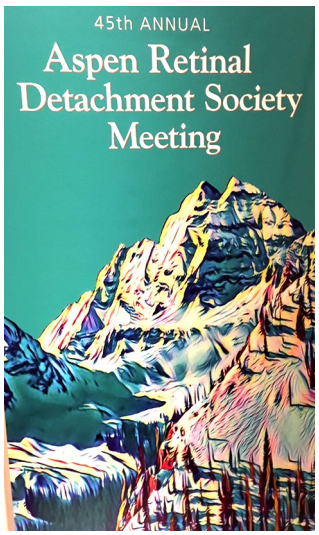
Marked learning of polypoidal choroidal vasculopathy in the audience of attendees during Dr. Kokame's presentation

Besides treatment with Lucentis, Eylea and Avastin, combination treatment with photodynamic treatment (PDT) has been recently shown to be very effective for PCV, especially when there is resistance to the above drugs. A recent study performed in Asia also showed that combined PDT and medication injection may be superior in vision results and in decreasing treatment burden rather than medication injections alone.

Hawaii provides a unique crossroads between Asia and the USA, which has allowed the development of close ties between leading researchers in Asia and the USA. The extensive experience with PCV in Asia has provided important expertise, which has allowed RCH to utilize the unique population in Hawaii to more accurately diagnose and treat this disease. The newest research has identified

Aspen Retina Continued...

a higher incidence of PCV in Caucasian patients with wet macular degeneration than previously recognized, which highlights the importance of more careful diagnostic testing to identify this disease, not only in Hawaii, but across the USA. PCV is important to recognize as different therapy may be considered, especially when PCV is resistant to the usual intravitreal injected medications.



The Aspen Retinal Detachment Society has become a highly respected meeting over the past 45 years, having been host to the most respected leaders and speakers in retinal disease. It is an honor for Dr. Kokame to have been invited to speak at this meeting for the third time. There were 120 retina specialists at this meeting, and there was excellent and spirited discussion of lecture topics, which is a hallmark of this meeting. One of the most discussed topics by the audience was the new information Dr. Kokame provided on his research on PCV. For Dr. Kokame, who is an avid skier, the meeting also provides an excellent venue to develop camaraderie among his colleagues throughout the USA on the ski slopes.

Dr. Kokame and retina colleagues skiing in Aspen, Colorado

Argus II Optical Coherence Tomography Study Group

The ARGUS II retinal prosthesis system ("bionic eye") has been FDA-approved since 2015 and has been implanted in over 100 patients across the United States. People who have gone blind due to retinitis pigmentosa have had a chance to regain partial vision with this new implant. Retina Consultants of Hawaii (RCH) has been fortunate enough to be the first center in the Asia-Pacific region to perform this special procedure.

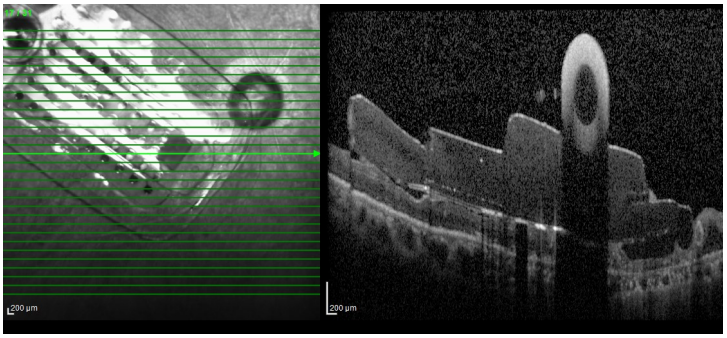
RCH was invited to participate in a collaboration study with other retina specialists across the United States and Europe. This study was led by Bascom Palmer Eye Institute, which is currently ranked as the country's top eye hospital, and is also where Dr. Kokame trained.

This retrospective study was designed to review images and data from 24 sites, both preoperatively and postoperatively. The goal was to use optical coherence tomography (OCT) to assess the placement and position of the microelectrode array and to correlate this potentially with visual function. Some of these studies may help with design of future implants. Other factors evaluated included macular edema, epiretinal membrane, and overlap of microelectrodes over the optic nerve.

Because there isn't an abundance of data on anatomic changes after implantation with the ARGUSII implant, it is interesting to see what was found. This study was presented at the Association of Research in Vision and Ophthalmology earlier this year and is expected to be presented at other major meetings like the American Academy of Ophthalmology later this year.

RCH has always enjoyed collaborative research with leading investigators around the world and around the nation. The remarkable photos below show a microelectrode array in good position across the macula. The OCT shows excellent apposition of the array to the retina., and also shows the appearance of the spring loaded tack holding the array in place.

RCH takes pride in collaborating with eye centers across the U.S and the rest of the world with the goal of learning and passing new knowledge that has yet to be discovered.



Optical coherence tomography after implantation of ARGUS II

Dr. Lai as Featured Speaker at Recent Medical Meetings

Dr. James Lai was recently the invited Keynote Speaker at the Taiwanese-American Medical Association Meeting held at the Oahu Country Club. The Taiwanese-American Medical Association Meeting is comprised of members from all specialties of medicine. Dr. Lai gave an update on Age-related Macular Degeneration (AMD), the leading cause of blindness in patients over the age of 60 in developed countries.

Retina Consultants of Hawaii (RCH) has been involved in all the latest national clinical trials for new treatments for wet AMD. Dr. Lai states, "By participating in these trials, RCH can stay at the cutting edge of new therapies. It has also allowed patients here in Hawaii to gain access to these novel treatments years before they are FDA approved and available to the public."

Dr. Lai was also the invited speaker at the recent Hawaii Ophthalmological Society meeting. At this meeting, Dr. Lai spoke about his experience with Iluvien, the latest drug approved for the treatment of diabetic macular edema (swelling in the retina). Iluvien is long-acting steroid implant that is injected directly into the eye and can last up to 3 years. Dr. Lai was the first in the state of Hawaii to implant this device into a patient and since then, Drs. Lai, Kokame and Wee have had the most experience in using this new drug in Hawaii. "Illuvien is an important addition to our treatment options for patients with diabetic macular edema. It is a game changer in terms of what we can offer patients who do not respond well to standard treatments, "states Dr. Lai.

Dr. James Lai speaking about the specialty of retina at the 2017 Taiwanese American Medical Association meeting

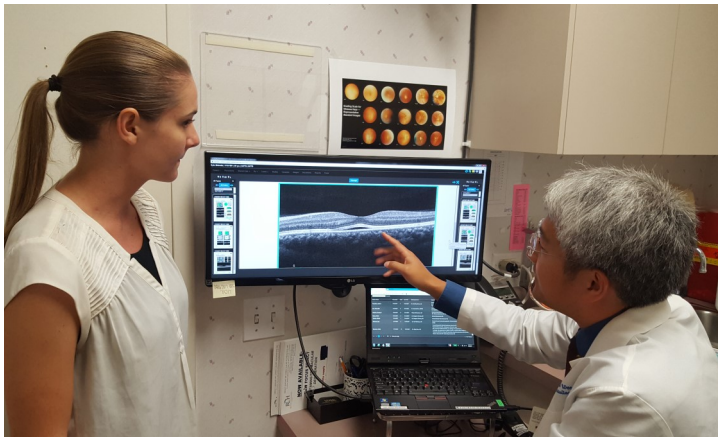
Dr. Wee Accepted into Clinical Faculty

Congratulations to Dr. Wee for his appointment to faculty member for the Department of Surgery at the University of Hawaii, John A. Burns School of Medicine. Faculty appointments are typically made based on a physician's accomplishments in teaching, research, service to the community, and clinical practice.

Dr. Wee has achieved this accomplishment not only by mentoring students, but also by functioning as a principal investigator for national clinical trials, volunteering for the internship admissions committee, and serving as an officer for the Hawaiian Ophthalmological Society. He explains that he "intends to continue making a positive impact both for patients and future students of medicine in Hawaii."

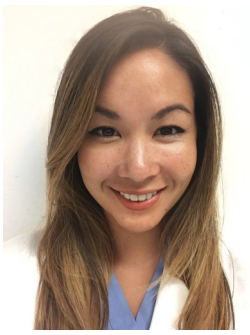
Both Dr. Lai and Dr. Kokame had previously been recognized for their time and dedication to teaching and research with faculty appointments in the Department of Surgery at the University of Hawaii, John A. Burns School of Medicine. Dr. Lai was recently promoted to Associate Clinical Professor while Dr. Kokame has attained Full Clinical Professorship. Dr. Wee's appointment as an Assistant Clinical Professor has allowed Retina Consultants of Hawaii to become fully intertwined with the well-recognized medical school in Honolulu.

The doctors of Retina Consultants of Hawaii are committed to teaching and mentoring the next generation of physicians for the state of Hawaii.



Dr. Wee reviewing significant findings on optical coherence tomography with first year medical student, Rebecca Lian

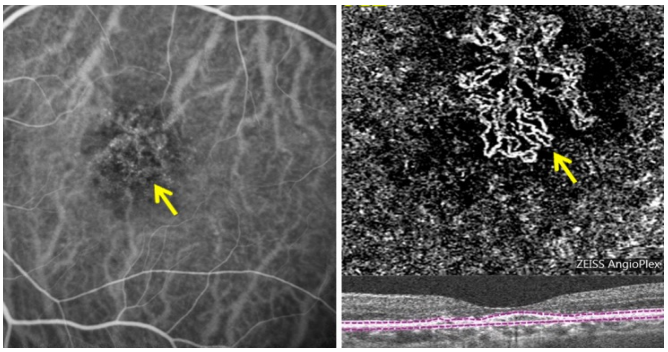
Ophthalmology for Future Hawaii



Talisa de Carlo is proud to be a local girl, born and raised in Honolulu, Hawaii. Her interest in ophthalmology first started freshman year at Punahou high school. She attended the University of Pennsylvania then earned her medical degree at Tufts University School of Medicine.

Dr. de Carlo did an Optical Coherence Tomography Fellowship with the New England Eye Center and the Massachusetts Institute of Technology where she investigated the exciting new technology optical coherence tomography angiography (OCTA). She has developed excellent experience and expertise helping to author approximately 40 publications on OCTA.

She is currently completing her transitional year internship at the John A. Burns School of Medicine. During this time, Dr. de Carlo has had the opportunity to continue her research endeavors with Drs. Kokame, Wee, and Lai at Retina Consultants of Hawaii (RCH). She has actively contributed to research projects involving polypoidal choroidal vasculopathy (PCV), an area of expertise and an intense research interest of RCH. She has made significant advances in comparing multiple diagnostic modalities for PCV, including OCTA, en face OCT, and indocyanine green angiography (ICGA). She has presented research from RCH at ophthalmic research meetings. As shown in the figures below, she demonstrated that in some cases, the newer OCTA below on the right can better image the subretinal vessels than the gold standard diagnostic method of ICGA, which requires an injection of dye.



Example of a polypoidal choroidal vasculopathy complex visualized better with optical coherence tomography angiography (right) versus Indocyanine green angiography (left)

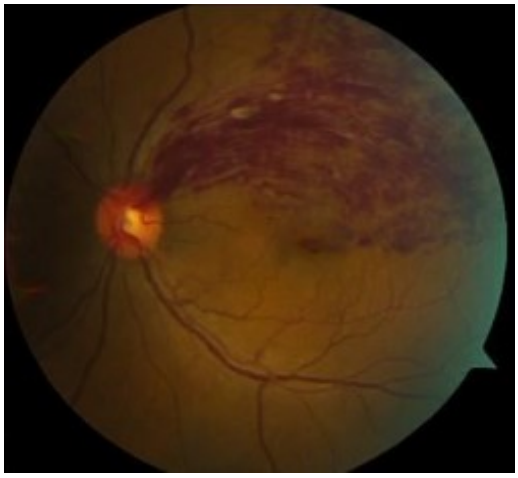
Dr. de Carlo also evaluates clinical trial images for the Boston Image Reading Center as a trained senior reader and is an invited reviewer for a variety of ophthalmology journals.

This summer, Dr. de Carlo will continue pursuing her dream to become an ophthalmologist by beginning her formal ophthalmology residency at the Illinois Eye and Ear Institute at the University of Illinois at Chicago. She has high hopes of returning to Hawaii to practice ophthalmology.

New Clinical Trial for Retinal Vein Occlusions

SAPPHIRE: A Randomized, Masked Controlled Trial to Study the **S**afety and Effic**a**cy of Su**p**rachoroidal CLS-TA in Conjunction with Intravitreal Aflibercep**t** in Subjects with **R**etina V**e**in Occlusion
Sponsor: Clearside Biomedical, Inc.
Principal Investigator: James C. Lai, MD

Retinal vein occlusions (RVO) are the second most common retinal vascular disease that causes visual impairment with an estimated 16.4 million adults being affected worldwide. This type of vascular disease results from a blockage in one of the veins that returns blood flow from the retina. The blockage then causes bleeding and swelling in the back of the eye which results in vision loss. Common risk factors for RVO include, age, diabetes, hypertension,

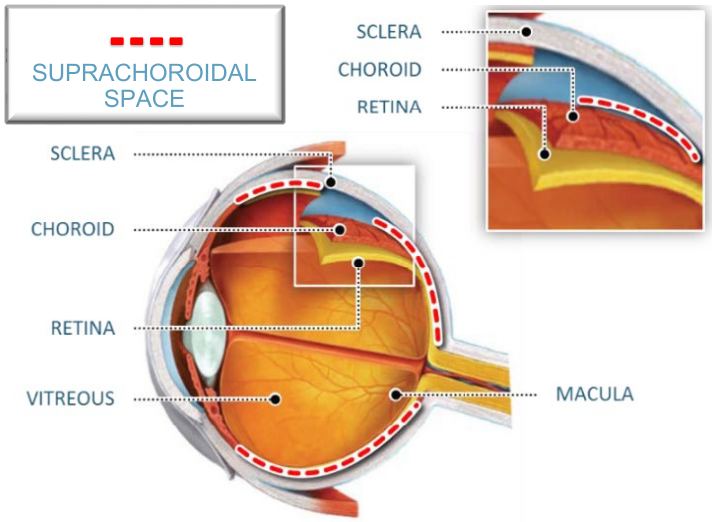


Fundus image of a branch retinal vein occlusion

high cholesterol, and smoking. Traditional treatments for this condition include laser therapy and more currently, intravitreal injections (injections into the eye) of either anti-vascular endothelial growth factors (anti-VEGF) or steroids. Intravitreal injections have dramatically improved the outlook for patients suffering from retinal vein occlusions. However, there is still room for improvement with the currently available medical treatments.

Retina Consultants of Hawaii (RCH) is pleased to have been selected as the only site in Hawaii for the SAPPHIRE study, a new Phase 3, 1-year clinical trial for a potentially new method of treatment for central and branch retinal vein occlusions.

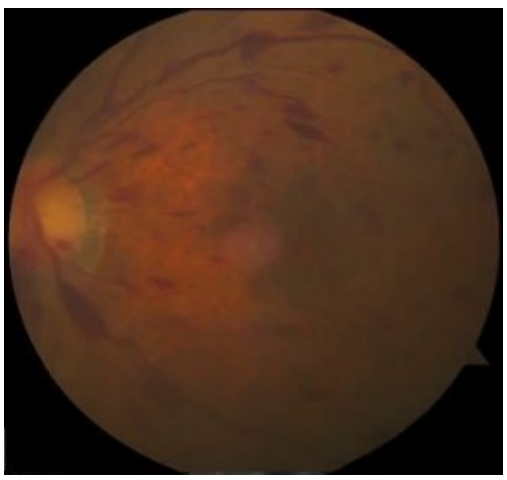
Clearside Biomedical has developed a novel drug delivery system for the eyes affected by retinal vein occlusions. In this two year clinical trial, standard intravitreal anti-VEGF injections will be compared to a combination of intravitreal anti-VEGF injections with a suprachoroidal injection of a steroid. The suprachoroidal space is the area of the eye between the sclera (white part of eye) and choroid (vascular region of the eye). By injecting medicines into the suprachoroidal space rather than the vitreous, the hope is that a higher concentration of medications will be delivered to the area of damaged tissue. Results from the Phase 2 Clinical Trial indicated that there was increased efficacy in terms of treating the vein occlusions with fewer overall needed injections and fewer side-effects to the medicines.



The suprachoroidal space is the area of the eye between the sclera and choroid illustrated as a red dotted line.

RCH is looking forward to providing a unique opportunity for newly diagnosed retinal vein occlusion patients who are looking to participate in this innovative treatment delivery system.

General Inclusion: Clinical diagnosis of RVO within 12 months of screening, treatment naïve, central sub-foveal thickness ≥ 300 µm, ETDRS BCVA score of ≥ 5 to ≤ 70 letters.



Fundus image of a central retinal vein occlusion

Ongoing Clinical Trials

RETINAL VEIN OCCLUSION: SAPPHIRE—Investigates the safety and efficacy of suprachoroidal triamcinolone acetonide with intravitreal aflibercept in treatment naïve retinal vein occlusions.

WET AMD: ONYX –Investigates the effectiveness of intravitreal REGN910-3 versus aflibercept, the current standard of care for treatment naïve wet macular degeneration.

WET AMD: MAKO –Investigates the effectiveness of topical Squalamine lactate ophthalmic solution in conjunction with monthly intravitreal ranibizumab for treatment naïve wet macular degeneration.

WET AMD: CEDAR– A study investigating the effectiveness of abicipar pegol every 2 or 3 months, versus ranibizumab for treatment naïve wet age-related macular degeneration.

WET AMD: HAWK—A study investigating the effectiveness of RTH258 every three months, compared to two months, versus aflibercept for treatment naïve Wet age-related macular degeneration.

DME: RUBY—Investigates the effectiveness of intravitreal REGN910-3 versus aflibercept, the current standard of care, for previously treated diabetic macular edema.

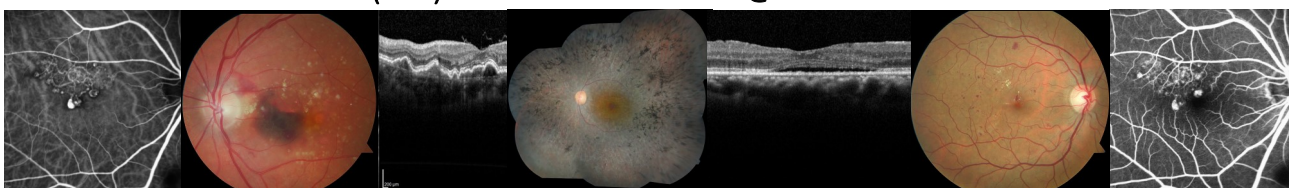
DME: PALADIN– Assesses the safety and intraocular pressure data in patients who have received the FDA-approved Iluvien for diabetic macular edema.

DRY AMD: OMASPECT—Open label extension study for the investigation of lampalizumab for dry age-related macular generation and geographic atrophy.

RETINITIS PIGMENTOSA: Post Approval Study for Argus II – Assesses the patient outcomes of the FDA-approved Argus II bionic eye.

PCV: HD-OCT Angiography Study– Dr. Gregg Kokame's independent study using the new Zeiss HD-OCT angiography technology to take non-invasive images of active polypoidal choroidal vasculopathy, compared to fluorescein and indocyanine angiography.

For questions or referrals, please contact our Research Department
at (808) 380-8060 or research@retinahi.com.



Completed Clinical Trials

PCV: EPIC Study—Dr. Gregg Kokame's independent study investigating the effectiveness of monthly or bi-monthly injections of aflibercept for patients that have previously or not previously received treatment for polypoidal choroidal vasculopathy.

WET AMD: LHA510—A study investigating the effectiveness of LHA510 topical therapy for the maintenance of previously treated wet age-related macular degeneration.

DRY AMD: CHROMA—Investigates the effectiveness of lampalizumab injections every 30-45 days in patients with dry age-related macular degeneration and geographic atrophy. There is no current FDA-proven treatment for Dry AMD.

VMA: ORBIT—A study assessing patient outcomes of FDA-approved Jetrea to treat vitreomacular adhesion.

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RCH

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Retina Consultants of Hawaii

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